REMARKS

Claims 1-42 are pending in the application. Claims 1, 2, 15, 17, 18, 21, 27 and 42 are under examination. Claims 3-13, 16, 19, 20, 23-26 and 30-38 have been previously cancelled. Claims 14, 22, 28, 29 and 39 are now cancelled. Claims 40 and 41 have been withdrawn.

Claim rejections - 35 U.S.C. § 112

Claims 1, 2, 14, 15, 17, 18, 21, 22, 27-29 and 39 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner did not find that the argument submitted on August 14, 2007 was persuasive, wherein it was submitted that three species of oligonucleotides disclosed in the instant application and two oligonucleotides provided in a Declaration filed October 5, 2006, which exemplified results for treatment and prophylactic effects in an appropriate animal model, provided adequate description for the genus comprising any oligonucleotide in length which provides antiviral activity by a non-sequence complementary mode of action. Still, the Examiner is of the opinion that the claims do not adequately describe the distinguishing features or attributes concisely shared by the members of the genus comprising oligonucleotides with non-sequence complementary mode of action and comprising any random sequences, whereby prevention and treatment of HSV-1, HSV-2 or CMV is obtained in an organism. The Examiner acknowledges that this specification teaches rather large differences in the abilities of various randomers to inhibit different viral infections, and each randomer is tested empirically because no concise description of common characteristics for this extensive genus has been provided. The disclosure of five effective oligonucleotides found to reduce or prevent viral infectivity of some strains of virus, with no common features, physical characteristics, or modes of action described or purportedly shared between them, does not provide adequate description for the genus of oligonucleotides claimed.

In this regard, the Applicants wish to submit that claims 1, 2 and 15 have been amended to define that the anti-viral activity of the oligonucleotide occurs principally by a sequence independent mode of action and that the oligonucleotide comprises all phosphorothioated linkages in order to clarify the genus with common features. Support can be found for example in paragraphs [0223] and [0357]. Regarding the restriction that all linkages are phosphorothioated, support can be found for example in Table 1 of the description and throughout the specification, as the active oligonucleotides are all phosphorothioated. Consequently, the distinguishing features or common attributes concisely shared by the members

of the genus claimed in the present application is that the oligonucleotides have at least 30 nucleotides in length, have an anti-viral activity occurring principally by a sequence independent mode of action (i.e. not sequence related or dependent) and comprises all phosphorothioated linkages. Applicants wish to further submit that the antiviral activity of the claimed oligonucleotide is due to the presence of the phosphorothioated linkages. A person skilled in the art would acknowledge that the oligonucleotides exemplified and claimed in the present application and also used in the Declaration of Dr. Jean-Marc Juteau enclosed herewith do not have any other common feature other than being at least 30 nucleotides in length (as exemplified in the application with REP 2005, REP 2006, REP 2007, REP 2008, SEQ ID NO: 6, SEQ ID NO: 9, REP 2024, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 26, REP 2060, SEQ ID NO: 22 and SEQ ID NO: 24), having an anti-viral activity occurring principally by a sequence independent mode of action and comprises all phosphorothioated linkages. Furthermore, since the oligonucleotides used in the present invention and claimed can be randomer oligonucleotides, as defined on page 14 of the present description, by the nature of the preparation used to produce them, sequence specific or complementary mode of action is irrelevant. In fact, it shows that the antiviral activity is not conferred by a specific sequence, but by any sequence having the now claimed characteristics, i.e. of being at least 30 nucleotides in length and being phosphorothioated. For example, in a 15 μmol preparation of a randomer oligonucleotide containing 31 nucleotides in length, this preparation will have at most 2 copies of every possible sequence of nucleotides. Thus, the presence of 2 copies of a specific sequence cannot account for the response observed in the present invention. Consequently, the antiviral activity of the oligonucleotides claimed in the present application and demonstrated for at least 14 different oligonucleotides *in vitro* (see Examples 1, 2 and 3 and Figs. 1-5, 7, 8, 11-18 and 37) and *in vivo* (see Declaration filed October 5, 2006 and also the Declaration enclosed herewith), is not due to a sequence specificity and complementary mode of action. Thus, Applicants are entitled to claim an oligonucleotide (without reference to a specific sequence) having an anti-viral activity occurring principally by a sequence independent mode of action and comprising all phosphorothioated linkages.

In view of the foregoing, reconsideration and withdrawal of the Examiner's rejection of the under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Rejection of claims 1, 2, 14, 15, 17, 18, 21, 22, 27-29 and 39 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is still maintained. Even

though it was previously argued that the full scope of the claims is enabled because the instant disclosure, at example 2 and figure 15, discloses various oligonucleotides with different lengths used to identify their efficacy as potential anti-HSV-2 molecules, the Examiner mentions that, in view of the evidence presented to her, these experiments are not representative of providing *in vivo* treatment or prophylaxis using a representative number of species of the expansive genus of nucleic acid molecules claimed. She only acknowledges that the specification teaches the *in vitro* inhibition of HSV-2 using oligonucleotides which are partially complementary to a target HSV-2 gene sequence. She also acknowledges that *in vivo* efficacy has been shown for the particularly described oligonucleotide, which is REP 2006, 2031 and 2107. The Examiner still feels that the ability to predict particular randomer's ability to treat or prevent a viral infection is highly unpredictable. The ability of two oligonucleotides to provide treatment effects of CMV and of two oligonucleotides to provide treatment or prophylactic effects for HSV-2 is not correlative or representative of the ability to predict the efficacy of any oligonucleotide of at least 30 nucleotides and with at least one phosphorothioated, acting in a non-complementary mode, to provide such prophylactic effects in a subject.

In this regard, Applicants wish to submit that claims 1, 2 and 15 have been amended to now define that the anti-viral activity of the oligonucleotide occurs principally by a sequence independent mode of action and that the oligonucleotide comprises all phosphorothioated linkages. It is thus believed that not only have the Applicants provided *in vitro* results demonstrating the antiviral activity of at least 14 different oligonucleotides of at least 30 nucleotides in length, having an anti-viral activity occurring principally by a sequence independent mode of action and that the oligonucleotide comprises all phosphorothioated linkages, but the results were correlated by the *in vivo* results demonstrating the efficacy of two oligonucleotides (REP 2006 and 2031) to prevent HSV-2 transmission in a mouse model, as well as three oligonucleotides (REP 2006, 2031 and 2107), to reduce CMV liver titers upon intraperitoneal administration have been disclosed. Consequently, Applicants believe that a reasonable correlation between the activity in question and the asserted utility has been demonstrated in the present application. A person skilled in the art would acknowledge that extensive data, reflecting a sufficient and/or representative number of varieties of species to reflect the complete genus, were disclosed in order to demonstrate the antiviral activity of the oligonucleotide of the present invention *in vitro*.

The Applicants also respectfully submit that the HSV-2 mouse model and the CMV mouse model used to demonstrate the ability of the oligonucleotides tested *in vivo* to treat or prevent HSV-2 and CMV are well accepted *in vivo* models for the study of pathogenesis and antiviral compound activity, as demonstrated in the references of Krmpotic *et al.* (2003, Microbes and Infection, 5: 1263-1277), Scott *et al.* (J General Virology, 86: 2141-2151), Bernstein *et al.* (2003, Antimicrobial Agents and Chemotherapy, 47: 3784-3788) and Bourne *et al.* (1999, J Infectious Diseases, 180: 203-205) submitted previously to the Examiner's attention.

In view of the foregoing, reconsideration and withdrawal of the Examiner's rejection of claims 1, 2, 14, 15, 17, 18, 21, 22, 27-29 and 39 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite because of the use of the expression "at least a portion". Claim 29 has been cancelled, thus rendering the Examiner's rejection moot.

Claim rejections - 35 U.S.C. § 103(a)

Claims 1, 2, 14, 15, 17, 18, 21, 22, 27-29, 39 and 42 have been rejected for allegedly being obvious in view of the teaching found in Sundquist et al., and in view of Trus et al. and McKay et al. The Examiner mentions that Sundquist et al. teach the use of SEQ ID NO: 24 for inhibiting viral assembly by interfering with requisite conformational changes that must occur in capsid formation, and teach approaches to inhibit capsid maturation, and hence teach inhibition of viral replication. The Examiner also points out that Trus et al. teach the importance of correct prohead assembly in viral capsid formation in HSV, and the conformational changes associated with capsid formation that are critical for viral maturation, viral particle formation and viral infectivity. Finally, the Examiner also points out that McKay et al. teach the incorporation of phosphorothioates, methyl phosphonates and 2'-O-sugar modifications for enhancing oligonucleotide stability. Consequently, the Examiner believes that it would have been obvious to one skilled in the art to use the oligonucleotide of SEQ ID NO: 24 for inhibiting capsid formation in a virus because Sundquist teaches SEQ ID NO: 24 for inhibiting viral assembly by interfering with capsid formation of a virus. In addition, the Examiner believes that one of ordinary skill in the art would have been motivated to test the previously-identified SEQ ID NO: 24 for its ability to inhibit capsid formation in other viruses, because both Sundquist and Trus teach the necessity of structural changes in capsid maturation in various viruses, and

vulnerability of viruses in disrupting this process, including HIV and HSV maturation. Finally, one ordinarily skilled in the art would have been motivated to incorporate the well-known modification of phosphorothioated in the oligonucleotide.

In this regard, the Applicants wish to first submit that claims 1, 2 and 15 have been amended to define the anti-viral activity of the oligonucleotide occurs principally by a sequence independent mode of action which differentiate the present invention from any prior art, for example prior art disclosing the use of sequence dependent aptamer and antisense, and differentiate from Sundquist (see explanation below). Support is found in [0223] and [0357] of the description. Further, claim 1 has been amended to define that the oligonucleotide does not comprises a TG-rich sequence (as supported in paragraph [0063] in the description). Claim 2 has been amended to define that the oligonucleotide inhibits a viral function selected from the group consisting of virus adsorption to a cell and virus infection into the cell (as supported in paragraphs [0168], [0160], [0161], [0227] and in the Declaration showing that the oligonucleotides of the present invention inhibit adsorption (binding) and infection into cell (entry) of herpesviridae species). In addition, claim 15 has also been amended to define that the oligonucleotide is selected not to form hairpins and not to have palindromic sequences contained therein (as supported in [0060]) to differentiate the encompassed oligonucleotides from antisense and from aptamers requiring tertiary structures.

Regarding the prior art, the Applicants submits that Sundquist describes the use of oligonucleotides made of alternating T and G. SEQ ID NO: 28 of Sundquist, referred by Examiner, is a (TG)n sequence, and thus not identical to SEQ ID NO: 24 as disclosed in the present application ($(AC)_{20}$ sequence). In Example 6 of Sundquist, it is clearly stated that the assembly of capsid-nucleocapsid (CA-NC) by oligonucleotides is "dependent on the sequence". Only (TG)n active oligos are described in Sundquist which can be used as a nucleic acid scaffold, which is not the case for the sequence disclosed in the present application. Further, the Applicants respectfully point out that nowhere in paragraphs [0003], p.6-7, [0088]-[0089] in Sundquist is there any reference to an oligonucleotide having antiviral activity. Thus, is it believed that Sundquist does not teach or suggest an oligonucleotide having an anti-viral activity occurring principally by a sequence independent mode of action and not comprising a TG-rich sequence, or inhibits a viral function selected from the group consisting of virus adsorption to a cell and virus infection into the cell, or that it is selected not to form hairpins and not to have palindromic sequences contained therein. The references of Trus et al. and McKay et al. do not

complement these deficiencies found in the reference of Sundquist. Consequently, the claims enclosed herewith are believed to be inventive in view of the teaching found in Sundquist, Trus et al. and McKay et al., taken alone or in combination. Reconsideration and withdrawal of the Examiner's rejection are earnestly solicited.

It is submitted, therefore, that the claims are in condition for allowance.

No additional fees are believed to be necessitated by this amendment. Should this be in error, authorization is hereby given to charge Deposit Account No. 19-5113 for any underpayment or to credit any overpayment.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully,

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Enc. Declaration of Dr. Jean-Marc Juteau.
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Extension of time